

Please amend the subject application as follows:

In the Claims

Please cancel Claims 2, 3, 6, 8, 11, 15, 16, 19, 21, 23, 28 and 36 without prejudice.

Please amend Claims 1, 4, 5, 7, 9, 10, 12, 14, 17, 18, 20, 22, 24, 25, 27, 29, 35, 37, 41, 44 and 47. Amendments to the claims are indicated in the attached "Marked Up Version of Amendments" (pages i - iv).

- B1
1. (Amended) A method of producing a mouse, wherein mouse non-inbred pluripotent ES cells are introduced into mouse tetraploid blastocysts by injection under conditions that result in production of an embryo and the resulting embryo is transferred into a foster mother which is maintained under conditions that result in development of live offspring, wherein said foster mother is a mouse.
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- B2
4. (Amended) The method of claim 1, wherein injection is piezo microinjection.
5. (Amended) A method of producing a mouse embryo comprising injecting mouse non-inbred ES cells into mouse tetraploid blastocysts and maintaining the resulting tetraploid blastocysts under conditions that result in formation of embryos, thereby producing a mouse embryo.
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- B3
7. (Twice Amended) The method of claim 5, wherein the mouse non-inbred ES cells are mutant mouse non-inbred ES cells and are injected into non-human tetraploid blastocysts by piezo microinjection.
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- B4
9. (Amended) A mouse produced by the method of claim 1.

10. (Amended) A mouse produced by the method of claim 4.
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- B5
12. (Amended) A mouse embryo produced by the method of claim 5.
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- B6 14. (Amended) A method of producing a mutant mouse, wherein mouse non-inbred pluripotent ES cells comprising at least one mutation in genomic DNA are introduced into mouse tetraploid blastocysts by injection under conditions that result in production of an embryo and the resulting embryo is transferred into a foster mother which is maintained under conditions that result in development of live offspring, thereby producing a mutant mouse, wherein said foster mother is a mouse.

- B7 17. (Amended) The method of claim 14, wherein injection is piezo microinjection.
18. (Amended) A method of producing a mutant mouse embryo comprising injecting mutant mouse non-inbred ES cells into mouse tetraploid blastocysts and maintaining the resulting tetraploid blastocysts under conditions that result in formation of embryos, thereby producing a mutant mouse embryo.

- B8 20. (Amended) The method of claim 18, wherein mutant mouse non-inbred ES cells are injected into mouse tetraploid blastocysts by piezo microinjection.

- B9 22. (Amended) A mutant mouse produced by the method of claim 14.

- B10 24. (Amended) A mutant mouse produced by the method of claim 17.

25. (Amended) A mutant mouse embryo produced by the method of claim 18.

- B11 27. (Amended) A method of producing a mutant mouse, comprising: (a) introducing mouse non-inbred ES cells comprising at least one mutation in genomic DNA into mouse tetraploid blastocysts by injection, thereby producing mouse blastocysts containing mouse non-inbred ES cells; (b) maintaining the product of (a) under conditions that result in production of embryos; (c) introducing an embryo into a pseudopregnant female mouse; and (d) maintaining the female mouse into which the embryo is introduced under

B11
cond conditions that result in development of live offspring, thereby producing a mutant mouse.

B12 29. (Amended) The method of claim 27, wherein injection is piezo microinjection.

B13 35. (Amended) A method of producing a mouse, comprising: (a) introducing mouse non-inbred ES cells into mouse tetraploid blastocysts by injection, thereby producing mouse blastocysts containing mouse non-inbred ES cells; (b) maintaining the product of (a) under conditions that result in production of embryos; (c) introducing an embryo into a pseudopregnant female mouse; and (d) maintaining the female mouse into which the embryo is introduced under conditions that result in development of live offspring, thereby producing a mouse.

B14 37. (Amended) The method of claim 35, wherein injection is piezo microinjection.

B15 41. (Twice Amended) A method of producing a mutant mouse, wherein mouse non-inbred pluripotent ES cells comprising at least one mutation in genomic DNA are introduced into mouse tetraploid blastocysts by injection under conditions that result in production of an embryo and the resulting embryo is transferred into a foster mother which is maintained under conditions that result in development of live offspring, wherein said foster mother is a mouse.

B16 44. (Twice Amended) A method of producing mouse XO F1 ES cells, comprising introducing into mouse male F1 ES cells a negative selection marker, under conditions appropriate for insertion of the negative selection marker in the Y chromosome of mouse male F1 ES cells, thereby producing a mixture of mouse male F1 ES cells comprising male F1 ES cells in which the negative selection marker is inserted in the Y chromosome and other male F1 ES cells, some of which do not contain a Y chromosome; subjecting the resulting mixture to conditions that result in the death of male F1 ES cells in which the Y chromosome has the negative selection marker inserted therein and do not result in